

Table 1-3                      A 28-day oral toxicity study of 2,6-di-tert-butyl-4-ethylphenol in rats with a recovery period of 2 weeks  
 Clinical signs (Recovery period)

Sex	Dose mg/kg	Findings	Day of recovery													
			1	2	3	4	5	6	7	8	9	10	11	12	13	14
Male	0	No. of animals	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	250	No. of animals	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6
Female	0	No. of animals	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	250	No. of animals	6	6	6	6	6	6	6	6	6	6	6	6	6	6
		No abnormality	6	6	6	6	6	6	6	6	6	6	6	6	6	6

Table 2-1 A 28-day oral toxicity study of 2,6-di-tert-butyl-4-ethylphenol in rats with a recovery period of 2 weeks  
Detailed clinical signs : home cage observations (Week 1)

Parameter	Sex	Male				Female			
	Dose (mg/kg)	0	15	60	250	0	15	60	250
	No. of animals	12	6	6	12	12	6	6	12
Posture Normal		12	6	6	12	12	6	6	12
Convulsion None		12	6	6	12	12	6	6	12
Abnormal behavior None		12	6	6	12	12	6	6	12

No significant difference in any treated groups from control group.

Table 2-2 A 28-day oral toxicity study of 2,6-di-tert-butyl-4-ethylphenol in rats with a recovery period of 2 weeks  
Detailed clinical signs : home cage observations (Week 2)

Parameter	Sex	Male				Female			
	Dose (mg/kg)	0	15	60	250	0	15	60	250
	No. of animals	12	6	6	12	12	6	6	12
Posture									
Normal		12	6	6	12	12	6	6	12
Convulsion									
None		12	6	6	12	12	6	6	12
Abnormal behavior									
None		12	6	6	12	12	6	6	12

No significant difference in any treated groups from control group.

Table 2-3

A 28-day oral toxicity study of 2,6-di-tert-butyl-4-ethylphenol in rats with a recovery period of 2 weeks  
 Detailed clinical signs : home cage observations (Week 3)

Parameter	Sex	Male				Female			
	Dose (mg/kg)	0	15	60	250	0	15	60	250
	No. of animals	12	6	6	12	12	6	6	12
Posture									
Normal		12	6	6	12	12	6	6	12
Convulsion									
None		12	6	6	12	12	6	6	12
Abnormal behavior									
None		12	6	6	12	12	6	6	12

No significant difference in any treated groups from control group.

Table 2-4 A 28-day oral toxicity study of 2,6-di-tert-butyl-4-ethylphenol in rats with a recovery period of 2 weeks  
Detailed clinical signs : home cage observations (Week 4)

Parameter	Sex	Male				Female			
		Dose (mg/kg)	0	15	60	250	0	15	60
	No. of animals	12	6	6	12	12	6	6	12
Posture	Normal	12	6	6	12	12	6	6	12
Convulsion	None	12	6	6	12	12	6	6	12
Abnormal behavior	None	12	6	6	12	12	6	6	12

No significant difference in any treated groups from control group.

Table 2-5 A 28-day oral toxicity study of 2,6-di-tert-butyl-4-ethylphenol in rats with a recovery period of 2 weeks  
Detailed clinical signs : home cage observations (Week 1 of recovery)

Parameter	Sex	Male		Female	
		Dose (mg/kg)	0	250	0
	No. of animals	6	6	6	6
Posture					
Normal		6	6	6	6
Convulsion					
None		6	6	6	6
Abnormal behavior					
None		6	6	6	6

No significant difference between treated group and control group.

Table 2-6 A 28-day oral toxicity study of 2,6-di-tert-butyl-4-ethylphenol in rats with a recovery period of 2 weeks  
Detailed clinical signs : home cage observations (Week 2 of recovery)

Parameter	Sex	Male		Female	
	Dose (mg/kg)	0	250	0	250
	No. of animals	6	6	6	6
Posture					
Normal		6	6	6	6
Convulsion					
None		6	6	6	6
Abnormal behavior					
None		6	6	6	6

No significant difference between treated group and control group.

Table 2-7

A 28-day oral toxicity study of 2,6-di-tert-butyl-4-ethylphenol in rats with a recovery period of 2 weeks  
Detailed clinical signs : in-the-hand observations (Week 1)

Parameter	Sex Dose (mg/kg) No. of animals	Male				Female			
		0	15	60	250	0	15	60	250
		12	6	6	12	12	6	6	12
Ease of removal from cage Easy		12	6	6	12	12	6	6	12
Fur condition Normal		12	6	6	12	12	6	6	12
Skin Normal		12	6	6	12	12	6	6	12
Secretions-Eye, Nose Absent		12	6	6	12	12	6	6	12
Exophthalmos Absent		12	6	6	12	12	6	6	12
Palpebral closure Normal		12	6	6	12	12	6	6	12
Mucosal membranes Normal		12	6	6	12	12	6	6	12
Lacrimation Normal		12	6	6	12	12	6	6	12
Piloerection Absent		12	6	6	12	12	6	6	12
Pupil size Normal		12	6	6	12	12	6	6	12
Salivation None		12	6	6	12	12	6	6	12
Abnormal respiration Absent		12	6	6	12	12	6	6	12
Reactivity to handling Easy		12	6	6	12	12	6	6	12

No significant difference in any treated groups from control group.



Table 2-8 A 28-day oral toxicity study of 2,6-di-tert-butyl-4-ethylphenol in rats with a recovery period of 2 weeks  
Detailed clinical signs : in-the-hand observations (Week 2)

Parameter	Sex	Male				Female			
	Dose (mg/kg)	0	15	60	250	0	15	60	250
	No. of animals	12	6	6	12	12	6	6	12
Ease of removal from cage									
Easy		12	6	6	12	11	6	6	12
Some resistance/avoidance		0	0	0	0	1	0	0	0
Fur condition									
Normal		12	6	6	12	12	6	6	12
Skin									
Normal		12	6	6	12	12	6	6	12
Secretions-Eye, Nose									
Absent		12	6	6	12	12	6	6	12
Exophthalmos									
Absent		12	6	6	12	12	6	6	12
Palpebral closure									
Normal		12	6	6	12	12	6	6	12
Mucosal membranes									
Normal		12	6	6	12	12	6	6	12
Lacrimation									
Normal		12	6	6	12	12	6	6	12
Piloerection									
Absent		12	6	6	12	12	6	6	12
Pupil size									
Normal		12	6	6	12	12	6	6	12
Salivation									
None		12	6	6	12	12	6	6	12
Abnormal respiration									
Absent		12	6	6	12	12	6	6	12
Reactivity to handling									
Easy		12	6	6	12	12	6	6	12

No significant difference in any treated groups from control group.

Table 2-9 A 28-day oral toxicity study of 2,6-di-tert-butyl-4-ethylphenol in rats with a recovery period of 2 weeks  
Detailed clinical signs : in-the-hand observations (Week 3)

Parameter	Sex	Male				Female			
	Dose (mg/kg)	0	15	60	250	0	15	60	250
	No. of animals	12	6	6	12	12	6	6	12
Ease of removal from cage									
Easy		12	6	6	12	11	6	5	12
Some resistance/avoidance		0	0	0	0	1	0	1	0
Fur condition									
Normal		12	6	6	12	12	6	6	12
Skin									
Normal		12	6	6	12	12	6	6	12
Secretions-Eye, Nose									
Absent		12	6	6	12	12	6	6	12
Exophthalmos									
Absent		12	6	6	12	12	6	6	12
Palpebral closure									
Normal		12	6	6	12	12	6	6	12
Mucosal membranes									
Normal		12	6	6	12	12	6	6	12
Lacrimation									
Normal		12	6	6	12	12	6	6	12
Piloerection									
Absent		12	6	6	12	12	6	6	12
Pupil size									
Normal		12	6	6	12	12	6	6	12
Salivation									
None		12	6	6	12	12	6	6	12
Abnormal respiration									
Absent		12	6	6	12	12	6	6	12
Reactivity to handling									
Easy		12	6	6	12	11	6	5	12
Slightly awkward		0	0	0	0	1	0	1	0

No significant difference in any treated groups from control group.

Table 2-10

A 28-day oral toxicity study of 2,6-di-tert-butyl-4-ethylphenol in rats with a recovery period of 2 weeks

Detailed clinical signs : in-the-hand observations (Week 4)

Parameter	Sex	Male				Female			
	Dose (mg/kg)	0	15	60	250	0	15	60	250
	No. of animals	12	6	6	12	12	6	6	12
Ease of removal from cage									
Easy		11	6	6	12	12	5	6	12
Some resistance/avoidance		1	0	0	0	0	1	0	0
Fur condition									
Normal		12	6	6	12	12	6	6	12
Skin									
Normal		12	6	6	12	12	6	6	12
Secretions-Eye, Nose									
Absent		12	6	6	12	12	6	6	12
Exophthalmos									
Absent		12	6	6	12	12	6	6	12
Palpebral closure									
Normal		12	6	6	12	12	6	6	12
Mucosal membranes									
Normal		12	6	6	12	12	6	6	12
Lacrimation									
Normal		12	6	6	12	12	6	6	12
Piloerection									
Absent		12	6	6	12	12	6	6	12
Pupil size									
Normal		12	6	6	12	12	6	6	12
Salivation									
None		12	6	6	12	12	6	6	12
Abnormal respiration									
Absent		12	6	6	12	12	6	6	12
Reactivity to handling									
Easy		12	6	6	12	11	6	6	11
Slightly awkward		0	0	0	0	1	0	0	1

No significant difference in any treated groups from control group.

Table 2-11

A 28-day oral toxicity study of 2,6-di-tert-butyl-4-ethylphenol in rats with a recovery period of 2 weeks  
 Detailed clinical signs : in-the-hand observations (Week 1 of recovery)

Parameter	Sex Dose (mg/kg) No. of animals	Male		Female	
		0	250	0	250
		6	6	6	6
Ease of removal from cage					
Easy		5	6	6	6
Some resistance/avoidance		1	0	0	0
Fur condition					
Normal		6	6	6	6
Skin					
Normal		6	6	6	6
Secretions-Eye, Nose					
Absent		6	6	6	6
Exophthalmos					
Absent		6	6	6	6
Palpebral closure					
Normal		6	6	6	6
Mucosal membranes					
Normal		6	6	6	6
Lacrimation					
Normal		6	6	6	6
Piloerection					
Absent		6	6	6	6
Pupil size					
Normal		6	6	6	6
Salivation					
None		6	6	6	6
Abnormal respiration					
Absent		6	6	6	6
Reactivity to handling					
Easy		6	6	6	6

No significant difference between treated group and control group.

Table 2-12

A 28-day oral toxicity study of 2,6-di-tert-butyl-4-ethylphenol in rats with a recovery period of 2 weeks  
 Detailed clinical signs : in-the-hand observations (Week 2 of recovery)

Parameter	Sex	Male		Female	
	Dose (mg/kg)	0	250	0	250
	No. of animals	6	6	6	6
Ease of removal from cage					
Easy		5	4	6	6
Some resistance/avoidance		1	0	0	0
Difficult		0	2	0	0
Fur condition					
Normal		6	6	6	6
Skin					
Normal		6	6	6	6
Secretions-Eye, Nose					
Absent		6	6	6	6
Exophthalmos					
Absent		6	6	6	6
Palpebral closure					
Normal		6	6	6	6
Mucosal membranes					
Normal		6	6	6	6
Lacrimation					
Normal		6	6	6	6
Piloerection					
Absent		6	6	6	6
Pupil size					
Normal		6	6	6	6
Salivation					
None		6	6	6	6
Abnormal respiration					
Absent		6	6	6	6
Reactivity to handling					
Easy		5	3	6	6
Slightly awkward		0	3	0	0
Difficult		1	0	0	0

No significant difference between treated group and control group.

Table 2-13

A 28-day oral toxicity study of 2,6-di-tert-butyl-4-ethylphenol in rats with a recovery period of 2 weeks  
 Detailed clinical signs : open field observation (Week 1)

Parameter	Sex	Male				Female			
	Dose (mg/kg)	0	15	60	250	0	15	60	250
	No. of animals	12	6	6	12	12	6	6	12
Arousal									
Normal		12	6	6	12	12	6	6	12
Convulsion									
None		12	6	6	12	12	6	6	12
Abnormal behavior									
None		12	6	6	12	12	6	6	12
Stereotypy									
None		12	6	6	12	12	6	6	12
Gait									
No/minimal location		0	0	0	1	0	0	0	0
Normal		12	6	6	11	12	6	6	12
Posture									
Normal		12	6	6	12	12	6	6	12
Grooming									
None		12	6	6	12	12	6	6	12
Rearing count (Mean±S.D.)		5± 3	5± 2	4± 3	4± 3	7± 2	4± 2	7± 2	6± 3
Defecation count (Mean±S.D.)		0± 1	0± 1	0± 1	1± 1	0± 0	0± 0	0± 0	0± 1
Urination									
None		9	3	5	10	12	6	4	11
Small amount		3	3	1	2	0	0	2	1

No significant difference in any treated groups from control group.

Table 2-14 A 28-day oral toxicity study of 2,6-di-tert-butyl-4-ethylphenol in rats with a recovery period of 2 weeks  
Detailed clinical signs : open field observation (Week 2)

Parameter	Sex	Male				Female			
	Dose (mg/kg)	0	15	60	250	0	15	60	250
	No. of animals	12	6	6	12	12	6	6	12
Arousal									
Normal		12	6	6	12	12	6	6	12
Convulsion									
None		12	6	6	12	12	6	6	12
Abnormal behavior						a)			
None		12	6	6	12	11	6	6	12
Minor		0	0	0	0	1	0	0	0
Stereotypy									
None		12	6	6	12	12	6	6	12
Gait									
No/minimal location		0	0	1	2	0	0	0	0
Normal		12	6	5	10	12	6	6	12
Posture									
Normal		12	6	6	12	12	6	6	12
Grooming									
None		12	6	6	12	12	6	6	12
Rearing count (Mean+S.D.)		5+ 3	4+ 2	4+ 3	2+ 2*D	7+ 4	6+ 4	9+ 4	6+ 3
Defecation count (Mean+S.D.)		0+ 0	0+ 0	0+ 0	1+ 1**DT	0+ 0	0+ 0	1+ 1	0+ 1
Urination									
None		10	6	6	10	12	6	6	9
Small amount		2	0	0	1	0	0	0	3
Moderate amount		0	0	0	1	0	0	0	0

a) Career  
\* : p<0.05 ; \*\* : p<0.01 (Significant difference from control group)  
D : Dunnett's test  
DT : Dunnett-type rank test

Table 2-15

A 28-day oral toxicity study of 2,6-di-tert-butyl-4-ethylphenol in rats with a recovery period of 2 weeks

Detailed clinical signs : open field observation (Week 3)

Parameter	Sex	Male				Female			
		Dose (mg/kg)	0	15	60	250	0	15	60
	No. of animals	12	6	6	12	12	6	6	12
Arousal									
Normal		12	6	6	12	12	5	6	12
Increased alertness		0	0	0	0	0	1	0	0
Convulsion									
None		12	6	6	12	12	6	6	12
Abnormal behavior									
None		12	6	6	12	12	6	5	11
Minor		0	0	0	0	0	0	1	1
Stereotypy									
None		12	6	6	12	12	6	6	12
Gait									
No/minimal location		1	1	0	1	0	0	0	0
Normal		11	5	6	11	12	6	6	12
Posture									
Normal		12	6	6	12	12	6	6	12
Grooming									
None		12	6	6	12	12	6	6	12
Rearing count (Mean±S.D.)		4± 3	2± 2	3± 3	3± 4	7± 3	5± 3	10± 5	6± 4
Defecation count (Mean±S.D.)		1± 2	1± 1	0± 0	2± 2	0± 1	0± 0	0± 0	0± 0
Urination									
None		10	4	5	8	12	6	6	10
Small amount		2	2	1	4	0	0	0	2

No significant difference in any treated groups from control group.



Table 2-16 A 28-day oral toxicity study of 2,6-di-tert-butyl-4-ethylphenol in rats with a recovery period of 2 weeks  
Detailed clinical signs : open field observation (Week 4)

Parameter	Sex	Male				Female			
	Dose (mg/kg)	0	15	60	250	0	15	60	250
	No. of animals	12	6	6	12	12	6	6	12
Arousal									
Normal		12	6	6	12	12	6	6	12
Convulsion									
None		12	6	6	12	12	6	6	12
Abnormal behavior									
None		12	6	6	12	12	6	6	12
Stereotypy									
None		12	6	6	12	12	6	6	12
Gait									
No/minimal location		2	1	1	0	0	0	0	0
Normal		10	5	5	12	12	6	6	12
Posture									
Normal		12	6	6	12	12	6	6	12
Grooming									
None		12	6	6	12	12	6	6	12
Rearing count (Mean±S.D.)		5± 3	4± 2	4± 3	5± 2	10± 3	8± 3	10± 4	7± 3*D
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	1± 1**DT	0± 0	0± 0	0± 0	0± 0
Urination									
None		11	6	6	9	12	6	6	12
Small amount		1	0	0	3	0	0	0	0

\* : p<0.05 ; \*\* : p<0.01 (Significant difference from control group)

D : Dunnett's test

DT : Dunnett-type rank test

Table 2-17

A 28-day oral toxicity study of 2,6-di-tert-butyl-4-ethylphenol in rats with a recovery period of 2 weeks  
Detailed clinical signs : open field observation (Week 1 of recovery)

Parameter	Sex	Male		Female	
	Dose (mg/kg)	0	250	0	250
	No. of animals	6	6	6	6
Arousal					
Normal		6	6	6	6
Convulsion					
None		6	6	6	6
Abnormal behavior					
None		6	6	6	6
Stereotypy					
None		6	6	6	6
Gait					
Normal		6	6	6	6
Posture					
Normal		6	6	6	6
Grooming					
None		6	6	6	6
Rearing count (Mean+S.D.)		6± 2	4± 2	8± 2	7± 3
Defecation count (Mean+S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		5	5	6	6
Small amount		0	1	0	0
Moderate amount		1	0	0	0

No significant difference between treated group and control group.

Table 2-18

A 28-day oral toxicity study of 2,6-di-tert-butyl-4-ethylphenol in rats with a recovery period of 2 weeks

Detailed clinical signs : open field observation (Week 2 of recovery)

Parameter	Sex	Male		Female	
	Dose (mg/kg)	0	250	0	250
	No. of animals	6	6	6	6
Arousal					
Normal		6	6	6	6
Convulsion					
None		6	6	6	6
Abnormal behavior					
None		6	6	6	6
Stereotypy					
None		6	6	6	6
Gait					
Normal		6	6	6	6
Posture					
Normal		6	6	6	6
Grooming					
None		6	6	6	6
Rearing count (Mean±S.D.)		5± 2	5± 2	8± 3	7± 2
Defecation count (Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Urination					
None		4	6	6	6
Small amount		1	0	0	0
Moderate amount		1	0	0	0

No significant difference between treated group and control group.

Table 2-19 A 28-day oral toxicity study of 2,6-di-tert-butyl-4-ethylphenol in rats with a recovery period of 2 weeks  
Manipulative test (Week 4)

Parameter	Sex	Male				Female			
	Dose (mg/kg)	0	15	60	250	0	15	60	250
	No. of animals	12	6	6	12	12	6	6	12
Auditory response Normal		12	6	6	12	12	6	6	12
Approach response Normal		12	6	6	12	12	6	6	12
Touch response Normal		12	6	6	12	12	6	6	12
Tail pinch response Normal		12	6	6	12	12	6	6	12
Pupillary reflex Pass, both		12	6	6	12	12	6	6	12
Aerial righting reflex (Total score: Mean+S.D.)		0± 0	0± 0	0± 0	0± 0	0± 0	0± 0	0± 0	0± 0
Landing foot splay (mm: Mean+S.D.)		78±16	89±15	91±16	89±17	62±13	61±19	64±28	68±14

No significant difference in any treated groups from control group.

Table 2-20 A 28-day oral toxicity study of 2,6-di-tert-butyl-4-ethylphenol in rats with a recovery period of 2 weeks  
Manipulative test (Week 2 of recovery)

Parameter	Sex	Male		Female	
	Dose (mg/kg)	0	250	0	250
	No. of animals	6	6	6	6
Auditory response					
Weak		0	1	0	1
Normal		6	5	6	5
Approach response					
Normal		6	6	6	6
Touch response					
Normal		6	6	6	6
Tail pinch response					
Normal		6	6	6	6
Pupillary reflex					
Pass, both		6	6	6	6
Aerial righting reflex (Total score: Mean±S.D.)		0± 0	0± 0	0± 0	0± 0
Landing foot splay (mm: Mean±S.D.)		72±14	91±13*T	52± 9	65±18

\* : p<0.05 (Significant difference from control group)

T : Student's t-test